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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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18M1/0702

EXAMINER

SCHWADRON R
ART UNIT PAPER NUMBER

1816

12

DATE MAILED:

07/02/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 4/9/97

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 11-14, 34-45 is/are pending in the application.
Of the above, claim(s) 14, 39, 42, 45 is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 11-13, 34-38, 40, 41, 43, 44 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s) _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

—SEE OFFICE ACTION ON THE FOLLOWING PAGES—

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15. Claims 11-13,34-38,40,41,43,44 are under consideration. Claim 33 has been cancelled. Claims 14,39,42,45 were withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 8, for the reasons elaborated in paragraph 15 of the previous Office Action. Regarding applicants comments on pages 5-7 of the amendment filed 4/9/97, in the event that the claims currently under consideration are found allowable, withdrawn claims will be treated as per M.P.E.P. section 821.04 (page 800-49, Rev. 2, July 1996).

RESPONSE TO APPLICANTS ARGUMENTS

16. Claims 35 and 36 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons elaborated in paragraph 23 of the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

There is no support in the specification as originally filed for the DNAs of claims 35 and 36.

Regarding applicants comments, the N-terminal amino acid sequence recited in claims 35 and 36 wherein Xaa consists of Val-Ala-Phe-Thr or Ala-Gln-Val-ala-Phe-Thr is not disclosed in the specification as originally filed. The specification discloses peptides containing the two aforementioned amino acid sequences, but said peptides consist of 21 or 30 amino acids respectively. The peptides recited in the claims containing the aforementioned amino acids are peptides of 13 and 15 amino acids which are not disclosed in the specification. While the peptides recited in the claims are found in the larger 21 or 30 amino acid peptides, the recitation of the aforementioned peptides in the claims results in a DNA that is broader in scope than that

disclosed in the specification (eg. encompasses DNAs encoding peptides not disclosed in the specification such as the 13 or 15 mer in combination with amino acids not disclosed in the specification).

17. Claims 11-13,33-38,40,41,43,44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

The specification as filed does not adequately teach how to make the claimed nucleic acids. It is well established that one cannot make that of which one has no conception. The specification discloses a partial protein sequence, and offers it up as enablement of nucleic acids encoding the isolated proteins and a broad range of other possible species. There is no disclosure of the complete sequence of any protein, nor is there any disclosure of even a single nucleic acid that would meet the limitations of the claims. Thus, there is no teaching of structure that the artisan could use as a guide in making the claimed nucleic acids. In the absence of any working examples, any guidance as to the structure of the claimed nucleic acids, and the unpredictability inherent in making nucleic acids to encode proteins which are defined almost solely by function, it would require undue experimentation to practice the claimed invention. It was found in Amgen v. Chugai, 18 USPQ 2d 1017 at 1021, that:

"A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. See Oka, 849 F. 2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method or preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having nor more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*,

until after the gene has been isolated."

This position was further supported in Fiers v. Sugano, where it was stated: "An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself" (26 USPQ2d 1601 at 1606). Thus, the instant specification does not adequately describe, and therefore *cannot* adequately teach how to make, the claimed invention. The Examiner also cites the decision In re Deuel, 34 USPQ2d 1210, in which it was found that disclosure of a partial protein sequence does not render obvious the DNA encoding that sequence; the situation here is analogous, in that applicants allege enablement of the claimed nucleic acids on the basis of the disclosure of a partial protein sequence, without having taught any particular structure for the claimed nucleic acids themselves.

Regarding claims 11,35 and 36, said claims recite functional properties of a particular protein encoded by a DNA wherein said DNA encompasses DNA other than the naturally occurring molecule. However, there is no disclosure in the specification of the particular region of the DNA that encodes that functional property. Thus it would require undue experimentation to produce the claimed DNAs because there is no guidance in the specification as to what portion of the DNA molecules encodes the particular domain mediating the functional activity. The claims encompass nucleic acids encoding innumerable muteins, variants, and derivatives. In the express absence of any information as to the complete structure of the encoded proteins, as well as any information as to the structure-function relationship of the proteins, it would require undue experimentation to practice the invention in a manner commensurate in scope with the claims, that is, to predict which of the innumerable encompassed nucleic acids would reasonably be expected to encode functional proteins.

The specification discloses an isolated protein(s) which share part of a common amino acid sequence near the amino terminus of the protein. Only a partial amino acid sequence is disclosed. The full amino acid sequence of the proteins is unknown. There is no disclosure in the specification as to whether the particular amino acid sequences listed on pages 23 are derived from the same molecule or that the molecule is found as four different but related molecules. There is no guidance in the specification as to whether the four potential forms of TBP-II are functionally active or the nature of the identity of the functionally active molecule. The specification proposes that using oligonucleotides, one can obtain DNA encoding the disclosed proteins. However, there

is no disclosure in the specification of the identity of said oligonucleotides. There is also no evidence of record that the amino acid sequence disclosed in the specification can be used to produce oligonucleotides that could have been used to isolate TBP-II DNA.

The Examiner notes that the description of claimed nucleic acids via a single biological function is similar to the situation in Ex parte Maizel (27 USPQ2d 1662 at 1665) in which it was found that:

Appellants have not chosen to claim the DNA by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in In re Hyatt, 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

In the instant case not only is the disclosure not commensurate in scope with the claims, the disclosure fails to present even a single operable species of the claimed invention.

Regarding applicants comments on page 12, last paragraph of the instant amendment, the claims under consideration in this application are drawn to DNA and vectors/host cells containing DNA. None of the claims under consideration are drawn to proteins. The claims under consideration are not drawn to DNA encoding a single protein. Claims 11-13,34,37,38,40,41 are drawn to any DNA (or cells/vectors containing said DNA) encoding a TBP-II binding protein containing the amino acid recited in said claim. Said claim encompasses DNAs encoding TBP-II binding protein irregardless of whether said proteins do or do not have the other characteristics disclosed in the specification for TBP-II binding protein(eg. a particular molecular weight or reactivity with polyclonal antibodies prepared against whole purified TNP-II as disclosed in Example 3 of the specification). Thus the claims encompass DNA encoding TBP-II that are not disclosed in the specification. Furthermore, based on the disclosure in the specification pages 23,24, it is unclear whether the claimed DNA encodes for one protein or several related proteins

of differing amino acid length with different N-terminal sequences. Thus, the claimed DNA does not encode one protein. Claims 35 and 36 also encompass DNAs that encompass proteins other than those specifically disclosed in the specification (eg. TNP-II other than with a particular molecular weight or reactivity with polyclonal antibodies prepared against whole purified TNP-II as disclosed in Example 3 of the specification). Regarding applicants comments about the specification, pages 23-24, if the molecules have differing N-terminal amino acid structures, than said molecules are different proteins, eg. they differ in amino acid structure. There is no disclosure in the specification as to whether there exists one TNP-II or several related molecules which differ in N-terminal amino acids. Applicants comments ignore the fact that molecules with differing amino acid sequences are different molecules. The reference to a "least truncated sequence" in page 24 of the specification does not mean that other shorter versions of said molecule do not exist. Furthermore, regarding the last two sequences disclosed in the specification on page 23, there is no disclosure that the amino acids encode proteins that would be present as part of the 30mer sequence disclosed on page 24 (eg. said sequences may or may not be derived from proteins having different amino acids at the C-terminal than those recite in the 30mer). There is no teaching in the specification that the various sequences recite in claims 35 and 36 are part of the same protein. Furthermore, all of the claims under consideration encompass DNAs encoding molecules with amino acid sequences other than the 30mer disclosed in page 24 of the specification, because all of the peptides recited in the claims are shorter than that molecule and encompass molecules that contain some of the amino acids disclosed in the 30mer in combination with other amino acids not disclosed in the 30mer. Regarding applicants comments about proteins, there are no claims drawn to proteins in the instant application that are under consideration.

Regarding applicants comments on page 15 of the instant amendment, the entire DNA sequence of TNP-II is not disclosed in the specification. Regarding applicants comments about PTO training materials, as per the quote on page 16 of the instant amendment, said quote refers to a protein wherein the entire amino acid sequence is known or disclosed in the specification. This is not the case in the instant application. Claims 11-13,34,37,38,40,41 are drawn to any DNA (or cells/vectors containing said DNA) encoding a TBP-II binding protein containing the amino acid recited in said claim. Said claim encompasses DNAs encoding TBP-II binding protein irregardless of whether said proteins do or do not have the other characteristics disclosed in the

specification for TBP-II binding protein(eg. a particular molecular weight or reactivity with polyclonal antibodies prepared against whole purified TNP-II as disclosed in Example 3 of the specification). Thus the claims encompass DNA encoding TBP-II that are not disclosed in the specification. While Ex parte Maizel relates to claims broader in scope than those under consideration, in both cases the DNAs are defined by a functional activity (eg. the DNA encodes a TBP-II) and wherein the claimed DNAs encode molecules that are not disclosed in the specification (eg. TBP-II of claims 11 wherein said molecule has amino acids other than disclosed in the intact 30mer disclosed in the specification or other functional properties not disclosed for TNP-II such as molecular weight or reactivity with a specific antibody). In addition, both the claims under consideration and those in Ex parte Maizel encompass DNAs wherein the intact DNA disclosing the claimed molecule is not disclosed in the specification. Regarding applicants comments on pages 16 and 17 of the instant amendment, none of the claims under consideration are drawn to proteins. Applicant is reminded that each US patent application is decided on its own merits. Regarding applicants comments on page 17, there is no evidence of record that the intact DNA sequence of TNP-II can be obtained using the particular amino acid sequences disclosed in the specification without undue experimentation. For example, the art recognizes that specific types of PCR probes with specific properties are required to clone a particular protein. There is no evidence of records that primers based on the disclosed amino acid sequences could be used for such a purpose. The full sequence of TBP-II is simply not disclosed in the specification. In re Deuel, 34 USPQ2d 1210, discloses that the partial protein sequence does not render obvious the DNA encoding that sequence; the situation here is analogous, in that applicants allege enablement of the claimed nucleic acids on the basis of the disclosure of a partial protein sequence, without having taught any particular structure for the claimed nucleic acids themselves. Further, the claims under consideration encompass DNA encoding TNP-II with properties other than those disclosed in the specification for TNP-II (differing molecular weight, amino acid sequences other than those encompassed by the 30mer disclosed in the specification, etc.). Regarding claims 11,35 and 36, said claims recite functional properties of a particular protein encoded by a DNA wherein said DNA encompasses DNA other than the naturally occurring molecule. However, there is no disclosure in the specification of the particular region of the DNA that encodes that functional property. Thus it would require undue experimentation to produce the claimed DNAs because there is no guidance in the specification as to what portion of the DNA

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molecules encodes the particular domain mediating the functional activity. The claims encompass nucleic acids encoding innumerable muteins, variants, and derivatives. In the express absence of any information as to the complete structure of the encoded proteins, as well as any information as to the structure-function relationship of the proteins, it would require undue experimentation to practice the invention in a manner commensurate in scope with the claims, that is, to predict which of the innumerable encompassed nucleic acids would reasonably be expected to encode functional proteins.

OTHER REJECTIONS

18. The following new grounds of rejection were necessitated by applicants amendment.

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371^o of this title before the invention thereof by the applicant for patent.

20. Claims 11-13,33-38,40,41,43,44 are rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al. (US Patent 5,395,760).

Smith et al. teach the claimed inventions (see Figure 2a and claims). This rejection can be overcome by the submission of English language copies of the foreign priority documents, assuming the claimed inventions are disclosed in said foreign priority documents.

21. No claim is allowed.

22. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office

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action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than **SIX MONTHS** from the date of this final action.

23. Papers related to this application may be submitted to Group 180 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 180 at (703) 305-7939.

24. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ms Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1800



Ron Schwadron, Ph.D.

Primary Examiner

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July 1, 1997